REMARKS

Claims 1-14, 16-23 and 27-32 are pending in this application. The Examiner withdrew claim 7-11, 13 and 19. The Applicants have amended claims 1, 20, 27-29, and 32, added new claim 33, and have cancelled claims 7-11, 13 and 19, without prejudice or disclaimer.

Upon entry of the present amendment, claims 1-6, 12, 14, 16-18, 20-23 and 27-33 are pending in this application.

I. Restriction under 35 U.S.C. 121 and 372

In accordance with 37 CFR 1.499, the Applicants were required to elect a single invention of the following inventions:

> Group I, claim(s) 5, 6, 12, 14, 16-18, and 21-23 (specifically) and claims 1-4 and 29-32 (generically), drawn to compounds wherein R4 is formulas 1, 2, 3 or 10 and R2 and R3 do not combine to make a ring.
>
> Group II, claim(s) 19 (specifically) and claims 1-2 and 29-32 (generically), drawn to compounds wherein R4 is formulas 1, 2, 3 or 10 and R2 and R3 make a ring.
>
> Group III, claim(s) 7, 10 and 13 (specifically) and claims 1-4 and 29-32 (generically), drawn to compounds wherein R4 is formulas 4, 5 or 6.
>
> Group IV, claim(s) 8, 9 and 11 (specifically) and claims 1-4 and 30-32 (generically), drawn to compounds wherein R4 is of formulas 7, 8 or 9.

The Applicants hereby elect Group I for prosecution on the merits, without traverse. Accordingly, the Applicants have deleted claims 7-11, 13, 19, as being drawn to non-elected subject matter. The Applicants preserve their right to file a divisional application directed to the cancelled non-elected subject matter in due course, without prejudice.

II. Rejection under 35 U.S.C. § 102(b) and § 103

The Office has rejected claims 1-6, 12, 14, 16-18, 21-23 and 29-32 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zeile (US Pat. No. 3,101,339), Nadelson (US Pat. No. 4,681,898), Bock (US Pat. No. 5,464,788), Dombro (CA 60:93472, 63: 35608), Diurno (CA 122:230112), Sekiya (CA 113: 190946, JP 02138161) and Sandoz (EP 0084292).

To anticipate a claim under 35 U.S.C. 102(b), a single source must contain all of the elements of the claim. *See Hybritech Inc.v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 U.S.P.Q. 81, 90 (Fed. Cir. 1986); *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984); *In re Marshall*, 578 F.2d 301, 304, 198 U.S.P.Q. 344, 346 (C.C.P.A. 1978).

To establish a *prima facie* case of obviousness, the PTO must satisfy three requirements. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. *See In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In re Skinner*, 2 U.S.P.Q. 2d 1788, 1790 (Bd. Pat. App. & Int 1986). "Obviousness cannot be established by combining the teachings of the prior art to product the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re Napier*, 55 F.3d 610, 613, 34 U.S.P.Q.2d 1782, 1784 (Fed. Cir. 1995)

Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. In other words, a hindsight analysis is not allowed. *See Amgen, Inc v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). In deciding obviousness one must look to the prior art from the vantage point in time prior to

when the claimed invention was made; hindsight obviousness after the invention has been made is not the test. *In re Carroll* (CCPA 1979) 601 F2d 1184, 202 USPQ 571.

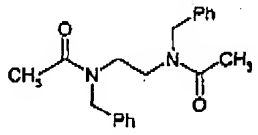
Lastly, the prior art reference or combination of references must teach or suggest all the limitation of the claims. *See In re Wilson*, 424 F.2ds 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). And the teachings or suggestions, as well as the expectation of success, must come from the prior art, not applicant's disclosure. *See In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir 1991).

The Applicants respectfully traverse the Office's rejection and contend that the present invention is not anticipated by or, in the alternative, obvious over Zeile, Nadelson, Bock, Dombro, Diurno, Sekiya and Sandoz.

The Office alleges that Zeile discloses compounds such as RN 10507-26-3 that anticipate the instantly claimed compounds and compositions and their use as CNS agents.

The Applicants respectfully submit that Zeile discloses quaternary amide derivatives of normorphine, which are useful as antagonists against the analgesic activity of morphine. The Zeile compounds all possess the normorphine ring skeleton, which is not present in the compounds of the present invention.

Additionally, the Applicants respectfully note that they have not been able to locate the compound, RN 10507-26-3 in Zeile, and suggest that the citation may be an error in Chemical Abstracts. Even if the compounds can be found in Zeile, the Applicants submit that the compound, RN 10507-26-3, which has the following structure:

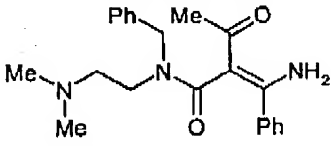


RN 10507-26-3

does not anticipate the claims of the present invention because R^2 and R^3 cannot be an acyl group.

As such, the Applicants respectfully submit that Zeile does not disclose every element of the claimed invention. Furthermore, there is no teaching or suggestion in Zeile to modify the reference in such a way that would result in the presently claimed invention.

The Office alleges that Nadelson discloses compounds and their use as pharmaceuticals for compounds such as RN 88098-99-1, which has the following structure:

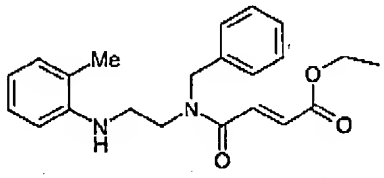


RN 88098-99-1

The Applicants respectfully submit that Nadelson discloses alkenamides which differ from the present invention by virtue of the carbonyl substituted alkenamide group. Thus, the present invention is not anticipated by Nadelson.

Furthermore, there is no suggestion or motivation in Nadelson that the carbonyl substituted alkenamide group could be replaced by a hydrogen atom or simple, unsubstituted alkyl or alkenyl group to provide further therapeutic agents. Thus, the present invention is not rendered obvious by the disclosure of Nadelson.

The Office alleges that Bock discloses compounds such as RN 170930-07-1, which has the following structure:



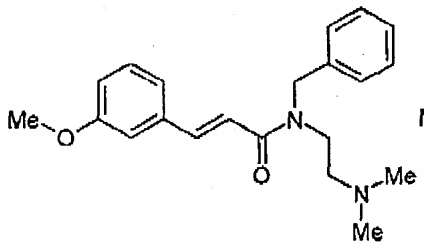
RN 170930-07-1

and its use as a pharmaceutical.

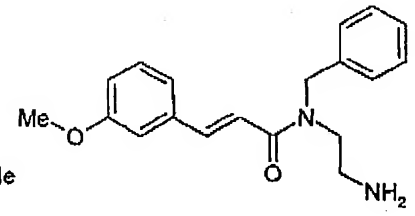
The Applicants respectfully submit that Bock discloses piperazine and spiro-piperidine derivatives that are structurally dissimilar to the compounds of the present invention. RN 170930-07-1 possesses a butenoic acid ethyl ester group in place of R^1 of the present invention. Thus, the present invention is not anticipated by Bock.

Contrary to the Examiner's assertion, RN 170930-07-1 is not disclosed for use as a pharmaceutical, but rather as the first intermediate in the synthesis of example 15. There is no suggestion in Bock that the compound RN 170930-07-1 could be modified by replacing the a butenoic acid ethyl ester group with a hydrogen atom or simple, unsubstituted alkyl or alkenyl group or that such a compound could possess therapeutic activity. Thus, the present invention is not rendered obvious by the disclosure of Bock.

The Office alleges that Dombro discloses compounds such as RN 10231-08-0 and RN 3115-15-9, which have the following structures:



RN 10321-08-0



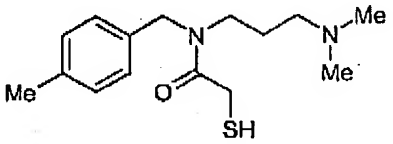
RN 3115-15-9

and their use as pharmaceuticals.

The Applicants respectfully submit that Dombro discloses cinnamamide derivatives as analogues of serotonin. Such compounds differ from the compounds of the present invention by the presence of the m-methoxy-styrene moiety. Thus, the present invention is novel over Dombro.

Furthermore, there is no suggestion in Dombro that the compounds could be modified by replacing the m-methoxy-styrene moiety with a hydrogen atom or simple, unsubstituted alkyl or alkenyl group to provide further therapeutic agents. Thus, the present invention is not obvious over the disclosure of Dombro.

The Office alleges that Diurno discloses compounds such as RN 162321-78-0, which has the following structure:



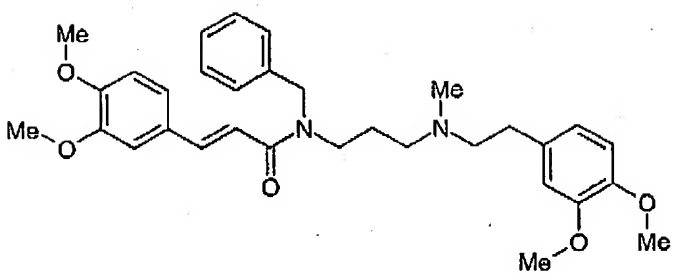
RN 162321-78-0

for use as a pharmaceutical.

The Applicants respectfully submit that Diurno discloses thiazolidinone derivatives, which are structurally dissimilar to the compounds of the present invention. Diurno also discloses chemical intermediates (such as RN 162321-78-0), which differ from the compounds of the present invention by the presence of the mercapto moiety. Thus, the present invention is not anticipated by Diurno.

Diurno discloses *thiazolidinone* derivatives for use as pharmaceuticals. Compounds such as RN 162321-78-0 have no therapeutic activity but are disclosed as intermediates for use in the preparation of the thiazolidinone derivatives. There is no suggestion in Diurno that the mercapto moiety could be replaced with a hydrogen atom or simple, unsubstituted alkyl or alkenyl group or that such modified compound might possess therapeutic activity. Thus, the present invention is not rendered obvious by Diurno.

The Office alleges that Sekiya discloses compounds such as RN 129989-57-7, which has the following structure:



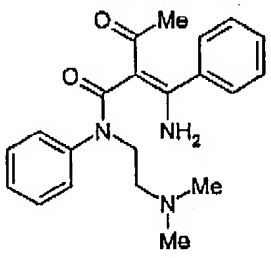
RN 129989-57-7

for use as a pharmaceutical.

The Applicants respectfully submit that Sekiya discloses cinnamamide derivatives for use as vasodilators. The cinnamamide compounds, such as RN 129989-57-7 differ from the compounds of the present invention by the presence of a substituted styrene moiety. RN 129989-57-7 also differs from the compounds of the present invention by virtue of the di-methoxy substituted phenylethyl moiety. Thus, the present invention is not anticipated by Sekiya.

Furthermore, there is no suggestion in Sekiya that the cinnamamide compounds could be modified by replacing the di-methoxy substituted styrene moiety with a hydrogen atom or simple, unsubstituted alkyl or alkenyl group. Thus, the present invention is not rendered obvious by the disclosure of Sekiya.

The Office alleges that Sandoz discloses many compounds within the scope of claims 1 that are used as pharmaceuticals. A representative compound has the following structure:



Compound No. 1

The Applicants respectfully submit that Sandoz discloses alkenamides which do not fall within the scope of claim 1 of the present invention. The compounds disclosed in Sandoz differ from the compounds of the present invention by virtue of the carbonyl substituted alkenamide group. Thus, the present invention is not anticipated by Sandoz.

Furthermore, there is no suggestion in Sandoz that the carbonyl substituted alkenamide or phenylalkenamide moiety could be replaced by a hydrogen atom or simple, unsubstituted alkyl or alkenyl group or that such compounds might possess therapeutic activity. Thus, the present invention is not rendered obvious by Sandoz.

For the reasons presented above, the Applicants submitted that the rejection under 35 U.S.C. 102(b) or, in the alternative, under 35 U.S.C. 103(a) has been overcome and respectfully request that the rejection be withdrawn.

III. Rejection under 35 U.S.C. § 112, second paragraph

The Office has rejected claims 20, 27 and 28 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

In response, the Applicants have revised claim 20 to correct a typographical error in the naming of the compound. The Applicants respectfully submit that the structure in Example 5 on page 18 of the specification, which is shown with the original name as found in claim 20, is the correct structure of the subject matter of claim 20. The naming of the compound in claim 20, as revised, clearly and unambiguously identifies the structure in Example 5.

The Applicants have also amended claims 27 and 28 to revise the dependency of the claims in accordance with the claim revisions presented in the preliminary amendment.

In light of the foregoing, the Applicants respectfully submit that the rejection of claims 20, 27 and 28 under 35 U.S.C. § 112, second paragraph, has been overcome and respectfully request that the rejection be withdrawn.

IV. Conclusion

Upon entry of the present amendments, the Applicants submit that this application is now in condition for allowance, which allowance is respectfully solicited.

If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-622-2658.

Respectfully submitted,

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